=> fil reg

FILE 'REGISTRY' ENTERED AT 17:35:25 ON 29 JAN 2002 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP'USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2002 American Chemical Society (ACS)

Jan Delaval Reference Librarian Biotechnology & Chemical Library CM1 1E07 – 703-308-4498 jan.delaval@uspto.gov

STRUCTURE FILE UPDATES: 28 JAN 2002 HIGHEST RN 387816-30-0 DICTIONARY FILE UPDATES: 28 JAN 2002 HIGHEST RN 387816-30-0

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the H/Z/CA/CAplus files between 12/27/01 and 1/23/02. Use of the P indicator in online and SDI searches during this period, either directly appended to a CAS Registry Number or by qualifying an L-number with /P, may have yielded incomplete results. As of 1/23/02, the situation has been resolved. Also, note that searches conducted using the PREP role indicator were not affected.

Customers running searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator between 12/27/01 and 1/23/02, are encouraged to re-run these strategies. Contact the CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698, worldwide, or send an e-mail to help@cas.org for further assistance or to receive a credit for any duplicate searches.

=> d ide can tot

L67 ANSWER 1 OF 7 REGISTRY COPYRIGHT 2002 ACS RN 9025-39-2 REGISTRY

CN Lyase, heparin (9CI) (CA INDEX NAME)

OTHER NAMES:

CN E.C. 3.2.1.19

CN E.C. 4.2.2.7

CN Heparin eliminase

CN Heparin lyase

CN Heparin lyase I

CN Heparinase

CN Heparinase I

DR 37290-85-0

MF Unspecified

CI MAN

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, PROMT, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

264 REFERENCES IN FILE CA (1967 TO DATE)

7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

266 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:58883

REFERENCE 2: 136:2475

```
REFERENCE
            3: 135:322723
                135:314489
REFERENCE
            4:
REFERENCE
            5:
                135:300403
REFERENCE
                135:286641
REFERENCE
            7:
                135:273169
REFERENCE
            8:
                135:179758
REFERENCE
            9:
                135:177020
REFERENCE 10:
                135:147424
L67
    ANSWER 2 OF 7 REGISTRY COPYRIGHT 2002 ACS
RN
     9005-49-6 REGISTRY
CN
     Heparin (8CI, 9CI)
                          (CA INDEX NAME)
OTHER NAMES:
     .alpha.-Heparin
CN
CN
     Bemiparin
CN
     Certoparin
CN
     Clexane
CN
     Clivarin
CN
     Clivarine
CN
     CY 216
CN
     CY 222
CN
     Dalteparin
CN
     Enoxaparin
CN
     Fluxum
CN
     FR 860
CN
     Fragmin A
     Fragmin B
CN
CN
     Fraxiparin .
CN
     Heparin sulfate
CN
     Heparinic acid
CN
     KB 101
CN
     Multiparin
CN
     Novoheparin
CN
     OP 386
CN
     OP 622
CN
     Pabyrn
CN
     Parnaparin
CN
     Parvoparin
CN
     Reviparin
CN
     Sandoparin
CN
     Sublingula
CN
     Vetren
CN
     Vitrum AB
DR
     9075-96-1, 11078-24-3, 11129-39-8, 104521-37-1, 37324-73-5, 91449-79-5
MF
     Unspecified
CI
     PMS, COM, MAN
PCT
     Manual registration, Polyester, Polyester formed
LC
                 ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,
       CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST,
       CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES,
       EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS,
       NAPRALERT, NIOSHTIC, PHAR, PHARMASEARCH, PIRA, PROMT, RTECS*, TOXCENTER,
       TOXLIT, USAN, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:
                      DSL**, EINECS**, WHO
         (**Enter CHEMLIST File for up-to-date regulatory information)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
```

17736 REFERENCES IN FILE CA (1967 TO DATE)

1770 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA 17754 REFERENCES IN FILE CAPLUS (1967 TO DATE)

```
136:74708
REFERENCE
REFERENCE
            2:
                136:74697
REFERENCE
                136:74695
REFERENCE
                136:74551
REFERENCE
                136:74543
REFERENCE
                136:70086
REFERENCE
            7:
                136:69730
REFERENCE
                136:68405
            8:
                136:67862
REFERENCE
REFERENCE 10:
                136:66177
    ANSWER 3 OF 7 REGISTRY COPYRIGHT 2002 ACS
     7783-20-2 REGISTRY
     Sulfuric acid diammonium salt (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN
     Ammonium sulfate
CN
     Ammonium sulfate ((NH4)2SO4)
CN
     Ammonium sulphate
CN
     Coaltrol LPA 40
CN
     Diammonium sulfate
CN
     Diammonium sulphate
CN
     Dolamin
CN
     Liase
     Nonnen R 999-10
CN
CN
     Para-Go
CN
     Sulfuric acid ammonium salt (1:2)
     Sulfuric acid, diammonium salt
CN
DR
     64006-53-7, 82168-61-4, 44071-93-4
MF
     H3 N . 1/2 H2 O4 S
CI
     COM
LC
                AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA,
     STN Files:
       CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM,
       CSNB, DDFU, DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE, ENCOMPLIT,
       ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*, HSDB*, IFICDB, IFIPAT,
       IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT,
       RTECS*, TOXCENTER, TOXLIT, TRCTHERMO*, TULSA, ULIDAT, USPAT2, USPATFULL,
       VETU, VTB
         (*File contains numerically searchable property data)
     Other Sources: DSL**, EINECS**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)
CRN
     (7664 - 93 - 9)
```

101 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

14588 REFERENCES IN FILE CA (1967 TO DATE)

```
14603 REFERENCES IN FILE CAPLUS (1967 TO DATE)
REFERENCE
            1:
                136:74698
REFERENCE
                136:73939
REFERENCE
            3:
                136:73590
REFERENCE
            4:
                136:72558
REFERENCE
            5:
                136:69070
REFERENCE
                136:68776
REFERENCE
            7:
                136:68774
REFERENCE
                136:68773
REFERENCE
            9:
                136:68767
REFERENCE 10:
                136:68754
L67
    ANSWER 4 OF 7 REGISTRY COPYRIGHT 2002 ACS
     7632-05-5 REGISTRY
     Phosphoric acid, sodium salt (8CI, 9CI) (CA INDEX NAME)
CN
OTHER NAMES:
CN
     Armite
CN
     Buromin
CN
     Hy-Phos
CN
     Instant Calgon
CN
     Phosphosoda
CN
     Sodium orthophosphate
CN
     Sodium phosphate
     Turrixin ST
CN
     12001-19-3, 8000-93-9
DR
MF
     H3 O4 P . x Na
CI
     COM
LC
                 ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA,
       CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN,
       DIOGENES, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*,
       IFICDB, IFIPAT, IFIUDB, MEDLINE, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA,
       PROMT, RTECS*, TOXCENTER, TOXLIT, TULSA, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
                      DSL**, EINECS**, TSCA**
```

CRN

(7664 - 38 - 2)

•x Na

2084 REFERENCES IN FILE CA (1967 TO DATE)
25 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2086 REFERENCES IN FILE CAPLUS (1967 TO DATE)

(**Enter CHEMLIST File for up-to-date regulatory information)

```
136:71864
REFERENCE
            1:
                136:58807
REFERENCE
            2:
REFERENCE
            3:
                136:57983
REFERENCE
                136:44493
REFERENCE
                136:31722
REFERENCE
                136:21956
REFERENCE
            7:
                136:21522
REFERENCE
            8:
                136:20551
REFERENCE
            9:
                136:8142
                136:2500
REFERENCE 10:
    ANSWER 5 OF 7 REGISTRY COPYRIGHT 2002 ACS
L67
RN
     3458-28-4 REGISTRY
     D-Mannose (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
     Mannose, D- (8CI)
OTHER NAMES:
CN
     (+)-Mannose
CN
     Carubinose
CN
     D(+)-Mannose
CN
     Mannose
CN
     Seminose
AR
     530-26-7
FS
     STEREOSEARCH
DR
     147-74-0
MF
     C6 H12 O6
CI
     COM
     STN Files:
                ADISNEWS, AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS,
LC
       BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS,
       CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DETHERM*, EMBASE, GMELIN*, HODOC*,
       IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT,
       NIOSHTIC, PIRA, PROMT, SPECINFO, SYNTHLINE, TOXCENTER, TOXLIT, TULSA,
       USPATFULL
         (*File contains numerically searchable property data)
     Other Sources: DSL**, EINECS**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)
```

Absolute stereochemistry. Rotation (+).

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

10556 REFERENCES IN FILE CA (1967 TO DATE)
527 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
10579 REFERENCES IN FILE CAPLUS (1967 TO DATE)
7 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

```
136:70024
            1:
REFERENCE
                136:69089
REFERENCE
            2:
                136:68810
REFERENCE
            3:
                136:68784
REFERENCE
            4:
REFERENCE
            5:
                136:68644
REFERENCE
            6:
                136:68377
REFERENCE
            7:
                136:66996
REFERENCE
            8:
                136:66914
REFERENCE
            9:
                136:66913
REFERENCE 10:
               136:66860
    ANSWER 6 OF 7 REGISTRY COPYRIGHT 2002 ACS
L67
RN
     99-20-7 REGISTRY
     .alpha.-D-Glucopyranoside, .alpha.-D-glucopyranosyl (9CI) (CA INDEX NAME)
CN
OTHER CA INDEX NAMES:
CN
     Trehalose (8CI)
OTHER NAMES:
     .alpha.,.alpha.'-D-Trehalose
CN
CN
     .alpha.,.alpha.-Trehalose
     .alpha.-D-Trehalose
CN
CN
     .alpha.-Trehalose
     D-(+)-Trehalose
CN
CN
     D-Trehalose
CN
     Ergot sugar
CN
     Mycose
CN
     Natural trehalose
CN
     Treha
CN
     Trehaose
FS
     STEREOSEARCH
DR
     229966-89-6
MF
     C12 H22 O11
CI
     COM
                  ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
LC
     STN Files:
       BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN,
       CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DETHERM*, DRUGU, EMBASE, GMELIN*,
       HODOC*, IFICDB, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, PIRA, PROMT,
       SPECINFO, TOXCENTER, TOXLIT, TULSA, USPATFULL
         (*File contains numerically searchable property data)
                      DSL**, EINECS**, TSCA**
     Other Sources:
         (**Enter CHEMLIST File for up-to-date regulatory information)
```

Absolute stereochemistry. Rotation (+).

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT 4709 REFERENCES IN FILE CA (1967 TO DATE) 262 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA 4723 REFERENCES IN FILE CAPLUS (1967 TO DATE) 64 REFERENCES IN FILE CAOLD (PRIOR TO 1967) REFERENCE 1: 136:77485 136:74683 REFERENCE 2: 136:74655 REFERENCE 3: 136:74308 REFERENCE 4: 136:69121 REFERENCE 5: 136:68768 REFERENCE 6: 136:67465 REFERENCE 7: REFERENCE 8: 136:66671 REFERENCE 9: 136:65213 REFERENCE 10: 136:58832 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2002 ACS RN **69-65-8** REGISTRY D-Mannitol (9CI) (CA INDEX NAME) OTHER CA INDEX NAMES: Cordycepic acid (6CI, 7CI) CN CN Mannitol, D- (8CI) OTHER NAMES: CN D-(-)-Mannitol CN Diosmol CN Isotol CN Maniton S CN Manna sugar CN Mannidex Mannigen CN CN Mannistol CN Mannit CN Mannite CN Mannitol CN Mannitolum CN Mannogem 2080 CN Marine Crystal CN Osmitrol CN Osmosal FS STEREOSEARCH DR 123897-58-5, 75398-80-0, 85085-15-0 MF CI COM ADISNEWS, AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, LC STN Files: BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PHARMASEARCH, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, TOXLIT, TULSA, USAN, USPAT2, USPATFULL, VETU (*File contains numerically searchable property data) DSL**, EINECS**, TSCA**

(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.

```
HO OH OH OH
```

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

10888 REFERENCES IN FILE CA (1967 TO DATE)

258 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

10921 REFERENCES IN FILE CAPLUS (1967 TO DATE)

2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

```
REFERENCE
             1:
                 136:74682
REFERENCE
             2:
                 136:74655
REFERENCE
             3:
                 136:74628
REFERENCE
             4:
                 136:74590
REFERENCE
                 136:74501
REFERENCE
                 136:69521
REFERENCE
             7:
                 136:69099
REFERENCE
             8:
                 136:69034
```

9:

10:

136:68875

136:67487

=> d his

REFERENCE

REFERENCE

(FILE 'HOME' ENTERED AT 17:16:53 ON 29 JAN 2002) SET COST OFF

FILE 'REGISTRY' ENTERED AT 17:17:05 ON 29 JAN 2002 E HEPARINASE/CN

```
1 S E3
L1
              3 S E5, E7, E9
L2
              2 S 9005-49-6 OR 9041-08-1
L3
                E GLUCONASE/CN
                E GLUCANASE/CN
              1 S E3
L4
L5
              2 S E24, E25
           1109 S GLUCANASE
L6
L7
           1106 S L6 NOT L4, L5
L8
             33 S L7 NOT SQL/FA
L9
             28 S L8 NOT MXS/ČI
L10
             18 S L9 AND GLUCANASE/INS.HP
             10 S L9 NOT L10
L11
L12
              1 S TREHALOSE/CN
             19 S C12H22O11/MF AND GLUCOPYRANOSIDE AND GLUCOPYRANOSYL
L13
             10 S L13 NOT (LABELED OR 11C# OR 13C# OR 14C# OR (D OR T)/ELS)
L14
              9 S L14 NOT OC4/ES
L15
L16
              9 S L12, L15
              3 S 69-65-8 OR 643-01-6 OR 133-43-7
L17
              3 S 3458-28-4 OR 10030-80-5 OR 40866-07-7
L18
```

```
E AMMONIUM SULFATE/CN
L19
              1 S E3
L20
            785 S 7664-93-9/CRN AND H3N
L21
             33 S L20 AND 2/NC
L22.
             15 S L21 AND H2O4S
             10 S L22 NOT (MNS/CI OR 15N OR 13N)
L23
L24
             25 S L16-L19, L23
L25
              1 S 7664-38-2
           1336 S 7664-38-2/CRN AND NA/ELS
L26
L27
             18 S L26 AND H304P AND 2/NC
L28
             13 S L27 NOT (FNA OR MNS/CI OR PROPANEDIOL)
L29
              1 S SODIUM CHLORIDE/CN
                E TRIS/CN
L30
              1 S E4
L31
             15 S L28, L29, L30
     FILE 'HCAPLUS' ENTERED AT 17:26:22 ON 29 JAN 2002
L32
            339 S L1 OR L2
L33
            991 S HEPARINASE
L34
             90 S HEPARIN LYASE
           1069 S L32-L34
L35
L36
              8 S L35 AND L24
L37
             17 S L35 AND (TREHALOSE OR MANNITOL OR MANNOSE OR AMMONIUM()(SULFA
L38
             17 S L36, L37
L39
              1 S L38 AND (L31 OR NACL OR (NA OR SODIUM) () CHLORIDE OR TRIS OR (
L40
              5 S L38 AND (L3 OR HEPARIN)
L41
              1 S L38 AND (L4 OR L5 OR L11 OR GLUCANASE)
L42
              5 S L39-L41
L43
              1 S L42 AND ADDITIVE
L44
              1 S L38 AND ADDITIVE
L45
              1 S L43, L44
          16745 S L35 OR L4 OR L5 OR L11 OR GLUCANASE
L46
L47
              1 S L38 AND (L31 OR NACL OR (NA OR SODIUM) () CHLORIDE OR TRIS OR (
L48
              1 S L45, L47
L49
            399 S L46 AND ADDITIVE
            908 S L46 AND STABIL?
L50
L51
             58 S L49 AND L50
             52 S L51 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)
L52
                E ANTIGNANI A/AU
L53
              2 S E4-E5
                E CHENG E/AU
L54
            237 S E3-E13, E51
                E EVANS J/AU
L55
            321 S E3,E35-E38
                E EVANS JEF/AU
             10 S E7, E14
L56
                E GRIPPI N/AU
L57
              2 S E4
                E WONG B/AU
L58
             39 S E3,E17,E18
                E WONG BRYAN/AU
L59
              7 S E5-E7
L60
           1562 S (BECTON OR DICKINSON)/PA,CS
              8 S L46 AND L53-L60
L61
L62
              1 S L61 AND L49
              2 S L61 AND STABIL?
L63
              2 S L62, L63
L64
L65
              1 S L64 NOT WINTERS ?/AU
L66
              1 S L48, L65
                SEL HIT RN
     FILE 'REGISTRY' ENTERED AT 17:35:09 ON 29 JAN 2002
L67
              7 S E1-E7
```

FILE 'REGISTRY' ENTERED AT 17:35:25 ON 29 JAN 2002

=> fil hcaplus FILE 'HCAPLUS' ENTERED AT 17:35:34 ON 29 JAN 2002 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications.

FILE COVERS 1907 - 29 Jan 2002 VOL 136 ISS 5 FILE LAST UPDATED: 28 Jan 2002 (20020128/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

HCAplus now provides online access to patents and literature covered in CA from 1907 to the present. Bibliographic information and abstracts were added in 2001 for over 3.8 million records from 1907-1966.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the H/Z/CA/CAplus files between 12/27/01 and 1/23/02. Use of the P indicator in online and SDI searches during this period, either directly appended to a CAS Registry Number or by qualifying an L-number with /P, may have yielded incomplete results. As of 1/23/02, the situation has been resolved. Also, note that searches conducted using the PREP role indicator were not affected.

DATE

19980807

19980811

EP 1998-114886

AU 1998-79892

CA 1998-2242693 19980709

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

=> d all 166

EP 902289

EP 902289

CA 2242693

AU 9879892

PΤ

```
ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
L66
AN
     1999:196433 HCAPLUS
DN
     130:220188
TТ
     Additive formulation comprising heparin-specific
     glucanase and use thereof
TN
     Antignani, Antoinette F.; Cheng, Emy; Evans,
     Jeffrey M.; Grippi, Nicholas A.; Wong, Bryan S.
PΑ
     Becton, Dickinson and Company, USA
SO
     Eur. Pat. Appl., 9 pp.
     CODEN: EPXXDW
DT
     Patent
LA
     English
IC
     ICM G01N033-86
     ICS C12Q001-56; B01L003-00; C12N009-88
CC
     9-16 (Biochemical Methods)
FAN.CNT 1
     PATENT NO.
                      KIND DATE
                                           APPLICATION NO.
```

A2

A3

IE, SI, LT, LV, FI, RO

AΑ

A1

19990317

20001220

19990304

19990318

```
JP 11139987
                       A2
                            19990525
                                            JP 1998-251604
                                                             19980904
                       В1
                            20010213
                                            US 1999-304382
     US 6187553
                                                             19990504
                      . A1
     US 2001001708
                            20010524
                                            US 2001-755269
                                                             20010105
PRAI US 1997-923838
                       Α
                            19970904
     US 1999-304382
                            19990504
                       Αl
     An additive formulation comprising heparinase and
AB
     trehalose, a method for using the formulation and a device contg.
     the formulation. The additive formulation is useful in
     substantially neutralizing residual heparin from a blood sample
     when used in a blood collection tube without interfering with the clin.
     anal. of the blood sample.
ST
     formulation comprising heparin glucanase
IT
     Apparatus
     Blood analysis
     Buffers
     Gamma ray
       Stabilizing agents
        (additive formulation comprising heparin-specific
        glucanase and use thereof)
IT
     Blood
        (collection tube; additive formulation comprising
        heparin-specific glucanase and use thereof)
IT
     69-65-8, D-Mannitol 99-20-7, Trehalose
                                      1333-74-0, Hydrogen, uses
     124-38-9, Carbon dioxide, uses
     3458-28-4, D-Mannose 7632-05-5, Sodium
     phosphate 7783-20-2, Ammonium sulfate
     , uses 9025-39-2, Heparinase
     RL: NUU (Other use, unclassified); USES (Uses)
        (additive formulation comprising heparin-specific
        glucanase and use thereof)
ΙT
     9005-49-6, Heparin, processes
     RL: PEP (Physical, engineering or chemical process); PROC (Process)
        (additive formulation comprising heparin-specific
        glucanase and use thereof)
=> fil wpix
FILE 'WPIX' ENTERED AT 17:43:07 ON 29 JAN 2002
COPYRIGHT (C) 2002 DERWENT INFORMATION LTD
                                             <20020128/UP>
FILE LAST UPDATED: 28 JAN 2002
                                       200206
                                                <200206/DW>
MOST RECENT DERWENT UPDATE
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE
     SDI'S MAY BE RUN ON EVERY UPDATE OR MONTHLY AS OF JUNE 2001.
     (EVERY UPDATE IS THE DEFAULT). FOR PRICING INFORMATION
     SEE HELP COST <<<
>>> FOR UP-TO-DATE INFORMATION ABOUT THE DERWENT CHEMISTRY
    RESOURCE, PLEASE VISIT
         http://www.derwent.com/chemistryresource/index.html <<<
>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<
=> d all abeq tech tot
L87
     ANSWER 1 OF 2 WPIX
                           COPYRIGHT 2002
                                             DERWENT INFORMATION LTD
     1999-169346 [15]
                        WPIX
AN
     N1999-123495
                        DNC C1999-049727
DNN
     New additive formulation comprising heparin-specific glucanase - useful
TΙ
     for neutralising residual heparin from blood sample.
DC
     B04 D16 S03
     ANTIGNANI, A F; CHENG, E; EVANS, J M; GRIPPI, N A; WONG, B S
IN
```

(BECT) BECTON DICKINSON & CO; (ANTI-I) ANTIGNANI A F; (CHEN-I) CHENG E;

PA

```
gitomer - 09 / 755269
     (EVAN-I) EVANS J M; (GRIP-I) GRIPPI N A; (WONG-I) WONG B S
CYC
    29
                                               9p
PΙ
     EP 902289
                   A2 19990317 (199915) * EN
                                                     G01N033-86
         R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
            RO SE SI
     AU 9879892
                   Α
                     19990318 (199923)
                                                     G01N033-48
                                              25p
     JP 11139987
                   A 19990525 (199931)
                                                     A61K038-46
     CA 2242693
                   A 19990304 (199933)
                                                     C12N009-88
     US 6187553
                   B1 20010213 (200111)
                                                     C12Q001-56
                                                                      <--
     US 2001001708 A1 20010524 (200130)#
                                                     C12N009-00
    EP 902289 A2 EP 1998-114886 19980807; AU 9879892 A AU 1998-79892 19980811;
ADT
     JP 11139987 A JP 1998-251604 19980904; CA 2242693 A CA 1998-2242693
     19980709; US 6187553 B1 Cont of US 1997-923838 19970904, US 1999-304382
     19990504; US 2001001708 A1 Cont of US 1999-304382 19990504, US 2001-755269
     20010105
PRAI US 1997-923838
                      19970904; US 1999-304382
                                                 19990504; US 2001-755269
     20010105
IC
     ICM
         A61K038-46; C12N009-00; C12N009-88; C12Q001-56; G01N033-48;
          G01N033-86
     ICS
          A61J001-05; B01L003-00
           902289 A UPAB: 19990416
AB
     EΡ
     NOVELTY - The additive formulation comprises a degradative glucanase
     enzyme specific for heparin and a stabiliser.
          DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
     following: (1) a method for eliminating the physiological effects of
     heparin on a blood components in a mixture of blood components and heparin
     in a blood collection tube comprising: (a) preparing the additive
     formulation as above; (b) spray coating the additive formulation to the
     inner wall of a blood collection tube; (c) drying the applied formulation
     by applying an airjet or forced air to the inner-wall of the coated tube
     at about 25-30 deg. C and for 5-10 minutes; (d) vacuum drying the
     inner-wall of the tube for 2 hours; (e) removing the oxygen from the
     inner-wall of the tube by back flushing the tube with gaseous mixture of
     CO2 and H2; (f) stoppering the tube; (g) irradiating the tubes within 2-5
     hours at 1.5 Mrads; (h) adding a blood sample containing heparin into the
     tube; (i) mixing the specimen in the tube with the additive formulation by
     about 5-10 manual conversions; and (j) allowing the specimen to clot; (2)
     a tube for preparing a heparin specimen for clotting comprising a top end,
     a bottom end, a side-well extending from the top end to the bottom end and
     including an exterior and interior surface, a spray coated additive
```

formulation comprising a mixture of a buffer, heparinase and trehalose on the interior surface of the tube; and (3) a method for making a tube for handling a heparin specimen for clotting comprising: (a) providing a container as above; (b) preparing the additive formulation comprising a mixture of sodium phosphate,

heparinase and trehalose; (c) dispensing the formulation to the inner wall surface of the tube in a fine mist; (d) drying the formulation by applying forced air; (e) vacuum drying the inner wall of the tube for about 2 hours at 35 deg. C at about 600 mm Hg; (f) removing oxygen from the tube by back flushing with a gaseous mixture of CO2/H2 at a mixture of about 80:20; (g) stoppering the tube; and (h) irradiating the tube and formulation by gamma irradiation.

USE - The additive formulation is useful as an additive in a tube to neutralise residual heparin in specimens taken from heparinised patients and accelerate clotting.

ADVANTAGE - The additive formulation is irradiation stable and achieves faster and more complete heparin neutralisation of heparinised blood therefore reducing the handling time required to manually remove heparin from patient specimens. It is also useful in removing heparin without interfering with the clinical analysis.

Dwg.0/2

FS CPÍ EPI

FA AB

MC CPI: B04-B04D5; B04-C02E1; B04-L06; B05-C01; B07-A02B; B10-A07; B11-C06;

B14-F08; D05-A02D; D05-C11

EPI: S03-E13D; S03-E14H1

```
L87
    ANSWER 2 OF 2 WPIX
                           COPYRIGHT 2002
                                            DERWENT INFORMATION LTD
AN
     1992-365996 [44] WPIX
DNC
    C1992-162475
     Eliminating physiological effects of heparin on blood components -
ΤI
     comprises treating blood contq. heparin with stabilised
     heparinase prepn., free of anticoagulant component.
DC
IN
     HEFT, R A; LEWIS, N T; ZIMMERMANN, J J
PΑ
     (IBEX) IBEX TECHNOLOGIES INC; (ZIMM-I) ZIMMERMANN J J; (IBEX-N) IBEX
     TECHNOLOGIES INC
CYC
PΙ
     WO 9217203
                   A1 19921015 (199244)* EN
                                              29p
                                                     A61K037-56
        RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE
         W: AU CA JP
     AU 9217713
                     19921102 (199305)
                                                     A61K037-56
     EP 537325
                   A1 19930421 (199316) EN
                                              29p
                                                     A61K037-56
         R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
     JP 05507297
                     19931021 (199347)
                                              29p
                                                     A61K037-54
     US 5262325
                   A 19931116 (199347)
                                               8p
                                                     C07K003-00
     US 5338677
                   A 19940816 (199432)
                                               g8
                                                     C12N009-24
                   B 19950413 (199524)
     AU 658418
                                                     A61K037-56
     JP 2542780
                   B2 19961009 (199645)
                                                     A61K035-14
     CA 2083162
                   C 19980811 (199843)
                                                     C12N009-88
                   B1 19991103 (199951)
     EP 537325
                                         EN
                                                     A61K038-51
        R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
     DE 69230243
                   E 19991209 (200004)
                                                     A61K038-51
                   T3 20000316 (200021)
     ES 2141106
                                                     A61K038-51
ADT
    WO 9217203 A1 WO 1992-US2724 19920403; AU 9217713 A AU 1992-17713
     19920403, WO 1992-US2724 19920403; EP 537325 A1 EP 1992-910865 19920403,
     WO 1992-US2724 19920403; JP 05507297 W JP 1992-510024 19920403, WO
     1992-US2724 19920403; US 5262325 A US 1991-680330 19910404; US 5338677 A
     Div ex US 1991-680330 19910404, US 1993-153134 19931115; AU 658418 B AU
     1992-17713 19920403; JP 2542780 B2 JP 1992-510024 19920403, WO 1992-US2724
     19920403; CA 2083162 C CA 1992-2083162 19920403; EP 537325 B1 EP
     1992-910865 19920403, WO 1992-US2724 19920403; DE 69230243 E DE
     1992-630243 19920403, EP 1992-910865 19920403, WO 1992-US2724 19920403; ES
     2141106 T3 EP 1992-910865 19920403
FDT
    AU 9217713 A Based on WO 9217203; EP 537325 Al Based on WO 9217203; JP
     05507297 W Based on WO 9217203; US 5338677 A Div ex US 5262325; AU 658418
     B Previous Publ. AU 9217713, Based on WO 9217203; JP 2542780 B2 Previous
     Publ. JP 05507297, Based on WO 9217203; EP 537325 B1 Based on WO 9217203;
     DE 69230243 E Based on EP 537325, Based on WO 9217203; ES 2141106 T3 Based
     on EP 537325
PRAI US 1991-680330
                      19910404
REP
     2.Jnl.Ref; EP 370958; WO 8705333; WO 8802400
IC
         A61K035-14; A61K037-54; A61K037-56; A61K038-51; C07K003-00;
          C12N009-88
         A61K038-46; C12N001-00; C12N001-12; C12Q001-56; G01N033-86
ICA
    C12N009-24; C12Q001-34
ICI
    C12N009-24, C12R001:20
AB
          9217203 A UPAB: 19931116
     Eliminating the physiological effects of heparin on blood components,
     comprises treating blood contg. heparin with a stabilised
     heparinase prepn., free of an anticoagulant component having
     optimal activity at pH of 6.7-7; NaCl concn. of 0.1, and 37
     deq.C.
          The heparinase may be purified from cultures of
     Flavobacterium heparinum by affinity chromatography using a polysulphated
     resin. The heparinase formulation may be prepd. by lyophilising
     0.05-3 IU of anticoagulant free heparinase in the presence of
     0.5-1 mg (NH4)2SO4/IU heparinase.
          A stabilised heparinase prepn., free of an anticoagulant
```

component, has optimal activity at pH of 6.5-7; NaCl concn. of

USE/ADVANTAGE - The heparinase prepn. can be used to

0.1, and 37 deg.C.

quickly and completely neutralise heparin over a wide range of concns. both in vitro and in vitro. The **heparinase** is free of coagulants altering coagulation times and is stable for an extended period of time at room temp. The **heparinase** is useful in vitro to eliminate the interference in haematological assays due to the presence of heparin. The herpainase is also useful for the in vivo neutralisation of heparin during surgical procedures.

Dwg.0/1

FS CPI

FA AB

MC CPI: B04-B02C3; B12-K04; D05-C08

ABEQ JP 05507297 W UPAB: 19940111

The elimination comprises treating blood contg. heparin with a stabilised heparinase prepn., free of an anticoagulant component having optimal activity at pH of 6.7-7; and NaCl concn. of 0.1, and 37 deg.C.

The heparinase may be pref purified from cultures of Flavobacterium heparinum by affinity chromatography using a polysulphated resin. The heparinase formulation may be prepd. by lyophilising 0.05-3 IU of anticoagulant free heparinase in 0.5-1 mg (NH4)2SO4(2SO4/IU heparinase.

A stabilised heparinase prepn. pref. free of an anticoagulant component, has optimal activity at pH of 6.5-7; and NaCl concn. of 0.1, and 37 deg.C.

USE/ADVANTAGE - The heparinase prepn. may be used to quickly and completely neutralise heparin over a wide range of concns. in vitro and in vitro. The heparinase is free of coagulants altering coagulation times and is stable for an extended period at room temp. Useful in vitro to eliminate the interference in haematological assays due to the presence of heparin. Also useful for the in vivo neutralisation of heparin during surgical procedures.

Dwg.0/1

ABEQ US 5262325 A UPAB: 19940111

Heparinase prepn. isolated from Flavobacterium heparinum contains no components that inhibit blood coagulation and is a reagent for eliminating heparin interference of the normal blood functions. The heparinase (but not an anticoagulant component) binds to a polysulphated resin at pH 7.0 (conductance 0.003-0.012 ohm-1).

Process for eliminating the physiol. effects of heparin in blood comprises contactng the blood with bacterial **heparinase**, opt. immobilised on a polysulphated resin (as above).

USE - The process facilitates invasive surgery and blood dialysis.

Dwg.0/1

Dwg.0/1

ABEQ US 5338677 A UPAB: 19940928

Heparinase isolated from Flavobacterium heparinum is free of anticoagulant activity. It has optimal activity of pH 6.5-7.0, salt concn. 0.1M and 37 deg. C..

USE/ADVANTAGE - Used as a clinical reagent to eliminate heparin interference of normal blood function. The **heparinase** is stable for at least 1 year, neutralises faster and more completely. Dwg.0/1

=> fil dpci

FILE 'DPCI' ENTERED AT 17:44:26 ON 29 JAN 2002 COPYRIGHT (C) 2002 DERWENT INFORMATION LTD

FILE LAST UPDATED: 18 JAN 2002 <20020118/UP>
MOST RECENT DERWENT DPCI UPDATE 200168
PATENTS CITATION INDEX, COVERS 1973 TO DATE

>>> SDI'S MAY BE RUN ON EVERY UPDATE OR MONTHLY AS OF JUNE 2001. (EVERY UPDATE IS THE DEFAULT). FOR PRICING INFORMATION SEE HELP COST <<<

LEARNING FILE LDPCI AVAILABLE <<< => d all tot L90 ANSWER 1 OF 2 DPCI COPYRIGHT 2002 DERWENT INFORMATION LTD 1999-169346 [15] DPCI DNN N1999-123495 DNC C1999-049727 ΤI New additive formulation comprising heparin-specific glucanase - useful for neutralising residual heparin from blood sample. DC IN ANTIGNANI, A F; CHENG, E; EVANS, J M; GRIPPI, N A; WONG, B S PA (BECT) BECTON DICKINSON & CO; (ANTI-I) ANTIGNANI A F; (CHEN-I) CHENG E; (EVAN-I) EVANS J M; (GRIP-I) GRIPPI N A; (WONG-I) WONG B S CYC 29 PΙ EP 902289 A2 19990317 (199915) * EN gę G01N033-86 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI AU 9879892 A 19990318 (199923) G01N033-48 JP 11139987 A 19990525 (199931) 25p A61K038-46 CA 2242693 A 19990304 (199933) C12N009-88 US 6187553 B1 20010213 (200111) C12Q001-56 <--US 2001001708 A1 20010524 (200130)# C12N009-00 ADT EP 902289 A2 EP 1998-114886 19980807; AU 9879892 A AU 1998-79892 19980811; JP 11139987 A JP 1998-251604 19980904; CA 2242693 A CA 1998-2242693 19980709; US 6187553 B1 Cont of US 1997-923838 19970904, US 1999-304382 19990504; US 2001001708 A1 Cont of US 1999-304382 19990504, US 2001-755269 20010105 PRAI US 1997-923838 19970904; US 1999-304382 19990504; US 2001-755269 20010105 IC A61K038-46; C12N009-00; C12N009-88; C12O001-56; G01N033-48; G01N033-86 ICS A61J001-05; B01L003-00 CPI EPI FS EXF EXAMINER'S FIELD OF SEARCH UPE: 20010504 NCL US 6187553 B1 20010213 000/435.130; 000/435.176; 000/435.177; 000/435.180; 000/435.188; 000/435.200; 000/435.269 CTCS CITATION COUNTERS _____ 0 PNC.DI Cited Patents Count (by inventor) PNC.DX Cited Patents Count (by examiner) IAC.DI Cited Issuing Authority Count (by inventor) IAC.DX 1 Cited Issuing Authority Count (by examiner) PNC.GI 0 Citing Patents Count (by inventor) PNC.GX 0 Citing Patents Count (by examiner) IAC.GI 0 Citing Issuing Authority Count (by inventor) IAC.GX Ω Citing Issuing Authority Count (by examiner) CRC.I O Cited Literature References Count (by inventor) CRC.X Cited Literature References Count (by examiner) UPD: '20010504 CDP CITED PATENTS Cited by Examiner

CITING PATENT CAT CITED PATENT ACCNO

US 6187553 B1 US 4891319 A 1987-021994/03

PA: (QUAD-N) QUADRANT BIORESOURCES LTD; (ROSE-I) ROSER B J

IN:

000/252.100; 435/200

ROSER, B J

```
US 5262325
                                           A 1992-365996/44
                    PA:
                         (IBEX) IBEX TECHNOLOGIES INC; (ZIMM-I) ZIMMERMANN J J;
                         (IBEX-N) IBEX TECHNOLOGIES INC
                         HEFT, R A; LEWIS, N T; ZIMMERMANN, J J
                             US 6010911
                                           A 1999-009450/01
                         (MEDT) MEDTRONIC INC
                    PA:
                         BAUGH, R F; LANE, C G; WILSON, A C
L90
    ANSWER 2 OF 2 DPCI COPYRIGHT 2002 DERWENT INFORMATION LTD
ΑN
     1992-365996 [44]
                        DPCI
DNC
     C1992-162475
TI
     Eliminating physiological effects of heparin on blood components -
     comprises treating blood contg. heparin with stabilised heparinase prepn.,
     free of anticoagulant component.
DC
ΙN
     HEFT, R A; LEWIS, N T; ZIMMERMANN, J J
PA
     (IBEX) IBEX TECHNOLOGIES INC; (ZIMM-I) ZIMMERMANN J J; (IBEX-N) IBEX
     TECHNOLOGIES INC
CYC
     19
PΙ
     WO 9217203
                   A1 19921015 (199244)* EN
                                               29p
                                                      A61K037-56
        RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE
         W: AU CA JP
     AU 9217713
                     19921102 (199305)
                                                      A61K037-56
                                               29p
     EP 537325
                   Al 19930421 (199316) EN
                                                      A61K037-56
         R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
     JP 05507297
                   W 19931021 (199347)
                                               29p
                                                      A61K037-54
     US 5262325
                   A 19931116 (199347)
                                               8p
                                                      C07K003-00
                                                                       <--
     US 5338677
                   A 19940816 (199432)
                                               q8
                                                      C12N009-24
     AU 658418
                   B 19950413 (199524)
                                                     A61K037-56
     JP 2542780
                   B2 19961009 (199645)
                                                     A61K035-14
                   C 19980811 (199843)
     CA 2083162
                                                      C12N009-88
     EP 537325
                   B1 19991103 (199951) EN
                                                     A61K038-51
         R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
     DE 69230243
                   E 19991209 (200004)
                                                     A61K038-51
                   T3 20000316 (200021)
                                                      A61K038-51
     ES 2141106
ADT
     WO 9217203 A1 WO 1992-US2724 19920403; AU 9217713 A AU 1992-17713
     19920403, WO 1992-US2724 19920403; EP 537325 A1 EP 1992-910865 19920403,
     WO 1992-US2724 19920403; JP 05507297 W JP 1992-510024 19920403, WO
     1992-US2724 19920403; US 5262325 A US 1991-680330 19910404; US 5338677 A
     Div ex US 1991-680330 19910404, US 1993-153134 19931115; AU 658418 B AU
     1992-17713 19920403; JP 2542780 B2 JP 1992-510024 19920403, WO 1992-US2724
     19920403; CA 2083162 C CA 1992-2083162 19920403; EP 537325 B1 EP
     1992-910865 19920403, WO 1992-US2724 19920403; DE 69230243 E DE
     1992-630243 19920403, EP 1992-910865 19920403, WO 1992-US2724 19920403; ES
     2141106 T3 EP 1992-910865 19920403
FDT
    AU 9217713 A Based on WO 9217203; EP 537325 A1 Based on WO 9217203; JP
     05507297 W Based on WO 9217203; US 5338677 A Div ex US 5262325; AU 658418
     B Previous Publ. AU 9217713, Based on WO 9217203; JP 2542780 B2 Previous
     Publ. JP 05507297, Based on WO 9217203; EP 537325 B1 Based on WO 9217203;
     DE 69230243 E Based on EP 537325, Based on WO 9217203; ES 2141106 T3 Based
     on EP 537325
PRAI US 1991-680330
                      19910404
     ICM A61K035-14; A61K037-54; A61K037-56; A61K038-51; C07K003-00;
IC
          C12N009-88
         A61K038-46; C12N001-00; C12N001-12; C12Q001-56; G01N033-86
ICA
    C12N009-24; C12Q001-34
ICI
    C12N009-24, C12R001:20
FS
     CPI
EXF
     EXAMINER'S FIELD OF SEARCH
                                  UPE: 19991212
    US 5338677
                   A 19940816
NCL
```

IC EP 537325 B1 19991103 A61K038-51

CTCS CITATION COUNTERS						
PNC.DI	0	Cited Patents Count (by inventor)				
PNC.DX	9	Cited Patents Count (by examiner)				
IAC.DI	0	Cited Issuing Authority Count (by inventor)				
IAC.DX	4	Cited Issuing Authority Count (by examiner)				
PNC.GI	1	Citing Patents Count (by inventor)				
PNC.GX	6	Citing Patents Count (by examiner)				
IAC.GI	1	Citing Issuing Authority Count (by inventor)				
IAC.GX	1	Citing Issuing Authority Count (by examiner)				
CRC.I	0	Cited Literature References Count (by inventor)				
CRC.X	31	Cited Literature References Count (by examiner)				
CDP CITED PATENTS		UPD: 19991212				

Cited by Examiner

•		
CITING PATENT	CA	T CITED PATENT ACCNO
EP 537325	A1	EP 370958 1990-165628/22
	PA:	(SHKJ) RES DEV CORP JAPAN; (RIKA) RIKAGAKU KENKYUSHO
	IN:	BELLAMY, W R; HORIKOSHI, K; BELLAMY, R W
		WO 8705333 A 1987-264129/37
	PA:	(CHIL-N) CHILDRENS MEDICAL CENT; (MASI) MASSACHUSETTS
		INST TECHNOLOGY; (CHIL-N) CHILDRENS MED CENT; (CHIL-N)
		CHILDRENS MED CORP; (MASI) MASSUCHUSETTS INST TECH
	IN:	FOLKMAN, J M; HANNAN, L R; LANGER, S R; THOMPSON, W R;
		FOLKMAN, M J; HANNAN, R L; LANGER, R S; THOMPSON, R W
		WO 8802400 A 1988-105519/15
	PA:	(MASI) MASSACHUSETTS INST TECHNOLOGY
	IN:	BERNSTEIN, H; COONEY, C L; LANGER, R S; YANG, V C
EP 537325	B1	EP 370958 A 1990-165628/22
	PA:	(SHKJ) RES DEV CORP JAPAN; (RIKA) RIKAGAKU KENKYUSHO
	IN:	BELLAMY, W R; HORIKOSHI, K; BELLAMY, R W
		WO 8705333 A 1987-264129/37
	PA:	(CHIL-N) CHILDRENS MEDICAL CENT; (MASI) MASSACHUSETTS
		INST TECHNOLOGY; (CHIL-N) CHILDRENS MED CENT; (CHIL-N)
		CHILDRENS MED CORP; (MASI) MASSUCHUSETTS INST TECH
	IN:	FOLKMAN, J M; HANNAN, L R; LANGER, S R; THOMPSON, W R;
		FOLKMAN, M J; HANNAN, R L; LANGER, R S; THOMPSON, R W
	D7.	WO 8802400 A 1988-105519/15 (MASI) MASSACHUSETTS INST TECHNOLOGY
	PA: IN:	BERNSTEIN, H; COONEY, C L; LANGER, R S; YANG, V C
JP 2542780	B2	JP 2057180 A 1990-060582/09
UP 2342700	PA:	(SEGK) SEIKAGAKU CORP; (SEGK) SEIKAGAKU KOGYO CO LTD
	IN:	KIKUCHI, H; MAEYAMA, K; YOSHIDA, K
	111.	JP 2503388 A 1986-322176/49
	PA:	(NIKR) NIPPON KOGAKU KK;
		' US 4863611 A 1989-332095/45
	PA:	(MASI) MASSACHUSETTS INST TECHNOLOGY
	IN:	BERNSTEIN, H; LANGER, R S; WHEATLEY, M A
US 5262325	Α	US 3950133 A 1973-26237U/19
	PA:	(MLCW) MALLINCKRODT CHEM WORKS
		US 4795703 A 1987-264129/37
	PA:	(CHIL-N) CHILDRENS MEDICAL CENT; (MASI) MASSACHUSETTS
		INST TECHNOLOGY; (CHIL-N) CHILDRENS MED CENT; (CHIL-N)
		CHILDRENS MED CORP; (MASI) MASSUCHUSETTS INST TECH
	IN:	FOLKMAN, J M; HANNAN, L R; LANGER, S R; THOMPSON, W R;
		FOLKMAN, M J; HANNAN, R L; LANGER, R S; THOMPSON, R W

US 5338677	A	US 3950133 A 1973-26237U/19
	PA:	(MLCW) MALLINCKRODT CHEM WORKS
,	•	US 4795703 A 1987-264129/37
	PA:	(CHIL-N) CHILDRENS MEDICAL CENT; (MASI) MASSACHUSETTS
		INST TECHNOLOGY; (CHIL-N) CHILDRENS MED CENT; (CHIL-N)
		CHILDRENS MED CORP; (MASI) MASSUCHUSETTS INST TECH
	IN:	FOLKMAN, J M; HANNAN, L R; LANGER, S R; THOMPSON, W R;
		FOLKMAN, M J; HANNAN, R L; LANGER, R S; THOMPSON, R W
WO 9217203	A1	EP 370958 1990-165628/22
	PA:	(SHKJ) RES DEV CORP JAPAN; (RIKA) RIKAGAKU KENKYUSHO
	IN:	BELLAMY, W R; HORIKOSHI, K; BELLAMY, R W
		WO 8705333 A 1987-264129/37
	PA:	(CHIL-N) CHILDRENS MEDICAL CENT; (MASI) MASSACHUSETTS
		INST TECHNOLOGY; (CHIL-N) CHILDRENS MED CENT; (CHIL-N)
		CHILDRENS MED CORP; (MASI) MASSUCHUSETTS INST TECH
		CHIEBRENO HED CORE, (HECT, HECCONOCETTE THOS TECH
	IN:	FOLKMAN, J M; HANNAN, L R; LANGER, S R; THOMPSON, W R;
	IN:	
	IN:	FOLKMAN, J M; HANNAN, L R; LANGER, S R; THOMPSON, W R;
	IN: PA:	FOLKMAN, J M; HANNAN, L R; LANGER, S R; THOMPSON, W R; FOLKMAN, M J; HANNAN, R L; LANGER, R S; THOMPSON, R W

REN LITERATURE CITATIONS UPR: 19991212

Citations by Examiner

CITING PATENT CAT	CITED LITERATURE
EP 537325 B1	Thrombosis Research, vol. 60, no. 4, 15 November 1990, L.H. BOeHMER et al.: "Heparin degradation by a novel microbial heparinase", pages 331-336, see page 331, paragraph 2 - page 332, paragraph 1; page 332, paragraph 2 - page 333, paragraph 1; page 334, paragraphs 1-2 (cited in the application)
EP 537325 B1	J. Lab. Clin. Med., vol. 79, no. 6, June 1972, E.D. HUTT et al.: "Use of heparinase to eliminate heparin inhibition in routine coagulation assays", pages 1027-1035, see page 1027, paragraph 1 - page 1028, paragraph 1; page 1028, paragraph 3; page 1029, paragraph 2 - page 1033, paragraph 1 (cited in the application)
US 5262325 A	Rosenberg, et al., "The purification and mechanism of action of the human antithrombin-heparin cofactor"; J. Biol. Chem., 248:6490-6505.
US 5262325 A	Cumming, A. M., et al., "In vitro neutralization of heparin in plasma prior to the activated partial thromboplastin time test; an assessment of four heparin antagonists and two anion exchange resins" Thrombosis Res., 41:43-56.
US 5262325 A	Sakamoto, et al., "Heparin and bone Metabolism: Effects of heparin on bone collagenase release and activity and an application of heparin-sepharose affiity chromatography for in vitro study of bone resorption" Chemistry and Biology of Heparin; (Elsevier/North Holland Press, Amsterdam 1981).
US 5262325 A	Hutt, Ed, et al., "Use of Heparinase to eliminate heparin inhibition in routine coagulation assays" J. Lab. Clin. Med. 79:1027, 1972.
US 5262325 A	Akoum, A., et al., "Anticoagulant activity of a bacterial glycopeptide" Thrombosis Res., 60: 9-18.
US 5262325 A	Funk, C., et al., "Reptilase-R_a new reagent in blood coagulation" Brit. J. Haematol., 21:43-52.
US 5262325 A	Bohmer, L. H., et al., "Heparin degradation by a novel heparinase" Thrombosis Res. 60:331-335.

US	5262325	A	Klein, et al., "Heparinase. Invivo activity and immunogenecity in rabbits" J. Lab. Clin. Med., 102:8280837.
110	E2C222E	71	
05	5262325	A	Langer, et al., "In vivo activity of microbial heparinase" Trans Am Soc Artific Intern Organs,
			28:387-390.
IIS	5262325	А	Fabian, et al. "Polycations as Possible
05	3202323	n	Substitutes for Protamine in Heparin
			Neutralization", Thrombosis Research, 17:239-247,
			(Pergamon Press Ltd. 1980).
US	5262325	Α	Langer, et al., "An Enzymatic System for Removing
~~	000000	••	Heparin in Extra-Corporeal Therapy", Science, vol.
			271, 261-263, (Jul. 16, 1982).
US	5262325	A	Dixon et al., Enzymes, Fractionation Methods, p.
			39, 1964.
US	5262325	A	Galliher, P. C., et al. "Heparinase production by
			Flavobacterium herpainum" Appl. Envir. Microbiol.,
			41(2):360-365.
US	5262325	A	Lindahl, et al., "Biosynthesis of Heparin" TIBS
			11(5):221-225, (1986).
US	5338677	A	Rosenberg, et al., "The purification and mechanism
			of action of the human anti-thrombin-heparin
			cofactor", J. Biol. Chem., 248:6490-6505
US	5338677	A	Choay, J., et al., "Anti-Xa active heparin
			oligosaccharides" Thrombosis Res., 11:240, 1980
US	5338677	A	Cumming, A. M. et al., "In vitro neutralization of
			heparin in plasma prior to the activated partial
			thromboplastin time test; an assessment of four
			heparin antagonists and two anion exchange resins"
			Thrombosis Res., 41:43-56
US	5338677	A	Funk, C., et al., "Reptilase-R-a new reagent in
		_	blood coagulation" Brit. J. Haematol., 21:43-52
US	5338677	A	Hutt, Ed, et al., "Use of Heparinase to eliminate
			heparin inhibition in routine coagulation assays"
110	E 2 2 0 C 7 7	70	J. Lab. Clin. Med. 79:1027, 1972
US	5338677	A	Akoum, A., et al., "Anticoagulant activity of a
m	5338677	Α	bacterial glycopeptide" Thrombosis Res., 60:9-18 Galliher, P. C., et al. "Heparinase production by
0.5	3330077	Α	Flavobacterium herpainum" Appl. Envir. Microbiol.
			41(2):360-365
US	5338677	Α	Bohmer, L. H., et al., "Heparin degradation by a
•		••	novel heparinase" Thrombosis Res. 60:331-335
US	5338677	A	Klein, et al., "Heparinase. Invivo activity and
			immunogenecity in rabbits" J. Lab Clin Med,
			102:8280837
US	5338677	A	Langer, et al., "In vivo activity of microbial
			heparinase" Trans Am Soc Artific Intern Organs,
			28:387-390
US	5338677	A	Fabian, et al. "Polycations as Possible
			Substitutes for Protamine in Heparin
			Neutralization", Thrombosis Research, 17:239-247,
			(Pergamon Press Ltd. 1980)
US.	5338677	A	Lander, et al., "An Enzymatic System for Removing
			Heparin in Extra-Corporeal Therapy", Science, vol.
	5000600		271, 261-263, (Jul. 16, 1982)
US	5338677	A '	Dixon et al., Enzymes, Fractionation Methods, p.
110	E 2 2 0 6 7 7	70	39, 1964
US	5338677	A	Lindahl, et al., "Biosynthesis of Heparin" TIBS
tro	E220677	75	11(5):221-225, (1986)
US	5338677	A	Sakamoto, et al., "Heparin and bone Metabolism: Effects of heparin on bone collagenase release and
			activity and an application of heparin-sepharose
			affiity chromatography for in vitro study of bone
			resorption" Chemistry and Biology of Heparin)
			(Elsevier/North Holland Press, Amsterdam 1981
			(LICOTIOI, HOLDIN HOLIGHAN I TOOD) THEOCOLAGE I JOI

```
CGP CITING PATENTS UPG: 20010612
------
```

Cited by Inventor

CITED PATENT CITING PATENT ACCNO

A WO 9534635 A1 1996-097381/10 US 5262325

PA: (IBEX-N) IBEX TECHNOLOGIES; (ZIMM-I) ZIMMERMANN J IN: BENNETT, C; BLAIN, F; GU, K; MUSIL, R; SU, H;

ZIMMERMANN, J

Cited by Examiner -----------

CITED PATENT CAT CITING PATENT ACCNO ______ US 5262325 A US 5919693 A 1996-097381/11 PA: (IBEX-N) IBEX TECHNOLOGIES; (ZIMM-I) ZIMMERMANN J; (ZIMM-I) ZIMMERMANN J J; (IBEX-N) IBEX TECHNOLOGIES CORP IN: BENNETT, C; BLAIN, F; GU, K; MUSIL, R; SU, H; ZIMMERMANN, J US 5972712 A 1999-009450/01 (MEDT) MEDTRONIC INC PA: IN: BAUGH, R F; LANE, C G; WILSON, A C US 5997863 A 1996-097456/11 PA: (IBEX-N) IBEX TECHNOLOGIES R & D INC; (ZIMM-I) ZIMMERMANN J; (IBEX-N) IBEX TECHNOLOGIES; (ZIMM-I) ZIMMERMANN J J BENNETT, D C; BROUGHTON, R; DANAGHER, P; VLODAVSKY, I; IN: ZIMMERMANN, J; BENNETT, D; BENNETT, C US 6187553 B1 1999-169346/11 (BECT) BECTON DICKINSON & CO PA: ANTIGNANI, A F; CHENG, E; EVANS, J M; GRIPPI, N A; WONG, B S US 6217863 B1 1997-272124/21 PA: (MASI) MASSACHUSETTS INST TECHNOLOGY COONEY, C L; ERNST, S; GODAVARTI, R; LANGER, R; TN: SASISEKHARAN, R; VENKATARAMAN, G B1 1997-272124/21 US 5338677 US 6217863 (MASI) MASSACHUSETTS INST TECHNOLOGY; PA: IN: COONEY, C L; ERNST, S; GODAVARTI, R; LANGER, R; SASISEKHARAN, R; VENKATARAMAN, G A 1995-206691/27 WO 9217203 US 5567417 Α1 (CHIL-N) CHILDRENS MEDICAL CENT; (MASI) MASSACHUSETTS PA: INST TECHNOLOGY COONEY, C L; LANGER, R S; MOSES, M A; NUGENT, M A; IN: SASISEKHARAN, R

=> d his

(FILE 'HOME' ENTERED AT 17:16:53 ON 29 JAN 2002) SET COST OFF

FILE 'REGISTRY' ENTERED AT 17:17:05 ON 29 JAN 2002

E HEPARINASE/CN

L11 S E3

L2 3 S E5, E7, E9

L3 2 S 9005-49-6 OR 9041-08-1

> E GLUCONASE/CN E GLUCANASE/CN

L41 S E3

L5 2 S E24, E25

```
1109 S GLUCANASE
L6
L7
           1106 S L6 NOT L4, L5
L8
             33 S L7 NOT SQL/FA
L9
             28 S L8 NOT MXS/CI
L10
             18 S L9 AND GLUCANASE/INS.HP
             10 S L9 NOT L10
L11
              1 S TREHALOSE/CN
L12
L13
             19 S C12H22O11/MF AND GLUCOPYRANOSIDE AND GLUCOPYRANOSYL
             10 S L13 NOT (LABELED OR 11C# OR 13C# OR 14C# OR (D OR T)/ELS)
L14
              9 S L14 NOT OC4/ES
L15
              9 S L12, L15
L16
              3 S 69-65-8 OR 643-01-6 OR 133-43-7
L17
L18
              3 S 3458-28-4 OR 10030-80-5 OR 40866-07-7
                E AMMONIUM SULFATE/CN
L19
              1 S E3
L20
            785 S 7664-93-9/CRN AND H3N
L21
             33 S L20 AND 2/NC
L22
             15 S L21 AND H204S
L23
             10 S L22 NOT (MNS/CI OR 15N OR 13N)
L24
             25 S L16-L19, L23
L25
              1 S 7664-38-2
           1336 S 7664-38-2/CRN AND NA/ELS
L26
L27
             18 S L26 AND H304P AND 2/NC
L28
             13 S L27 NOT (FNA OR MNS/CI OR PROPANEDIOL)
              1 S SODIUM CHLORIDE/CN
L29
                E TRIS/CN
L30
              1 S E4
L31
             15 S L28, L29, L30
     FILE 'HCAPLUS' ENTERED AT 17:26:22 ON 29 JAN 2002
L32
            339 S L1 OR L2
L33
            991 S HEPARINASE
L34
             90 S HEPARIN LYASE
L35
           1069 S L32-L34
L36
              8 S L35 AND L24
L37
             17 S L35 AND (TREHALOSE OR MANNITOL OR MANNOSE OR AMMONIUM() (SULFA
L38
             17 S L36, L37
L39
              1 S L38 AND (L31 OR NACL OR (NA OR SODIUM) () CHLORIDE OR TRIS OR (
              5 S L38 AND (L3 OR HEPARIN)
L40
L41
              1 S L38 AND (L4 OR L5 OR L11 OR GLUCANASE)
              5 S L39-L41
L42
L43
              1 S L42 AND ADDITIVE
L44
              1 S L38 AND ADDITIVE
L45
              1 S L43, L44
L46
          16745 S L35 OR L4 OR L5 OR L11 OR GLUCANASE
L47
              1 S L38 AND (L31 OR NACL OR (NA OR SODIUM) () CHLORIDE OR TRIS OR (
L48
              1 S L45, L47
L49
            399 S L46 AND ADDITIVE
L50
            908 S L46 AND STABIL?
L51
             58 S L49 AND L50
L52
             52 S L51 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)
                E ANTIGNANI A/AU
L53
              2 S E4-E5
                E CHENG E/AU
L54
            237 S E3-E13, E51
                E EVANS J/AU
L55
            321 S E3,E35-E38
                E EVANS JEF/AU
L56
             10 S E7, E14
                E GRIPPI N/AU
L57
              2 S E4
                E WONG B/AU
L58
             39 S E3, E17, E18
                E WONG BRYAN/AU
              7 S E5-E7
L59
L60
           1562 S (BECTON OR DICKINSON)/PA,CS
```

```
L61
               8 S L46 AND L53-L60
               1 S L61 AND L49
L62
L63
               2 $ L61 AND STABIL?
L64
               2 S L62, L63
               1 S L64 NOT WINTERS ?/AU
L65
L66
               1 S L48, L65
                 SEL HIT RN
      FILE 'REGISTRY' ENTERED AT 17:35:09 ON 29 JAN 2002
               7 S E1-E7
L67
      FILE 'REGISTRY' ENTERED AT 17:35:25 ON 29 JAN 2002
      FILE 'HCAPLUS' ENTERED AT 17:35:34 ON 29 JAN 2002
      FILE 'WPIX' ENTERED AT 17:35:47 ON 29 JAN 2002
                 E US6187553/PN
L68
               1 S E3
L69
              77 S HEPARINASE
              39 S HEPARANASE
L70
             107 S L69,L70
L71
               2 S L71 AND (TREHALOSE OR MANNITOL OR MANNOSE OR AMMONIUM()(SULFA
L72
                 E TREHALOSE/DCN
                 E E3+ALL
L73
               0 S L71 AND E2
                 E MANNITOL/DCN
                 E E3+ALL
L74
               0 S L71 AND (E2 OR 0290/DRN)
L75
               0 S L71 AND E6
                 E MANNOSE/DCN
                 E E3 ALL
                 E MANNOSE/DCN
                 E E3+ALL
L76
               0 S L71 AND (E2 OR 1616/DRN)
                 E AMMONIUM SULFATE/DCN
                 E E3 ALL
                 E AMMONIUM SULFATE/DCN
                 E E3+ALL
. L77
               0 S L71 AND (E2 OR 1786/DRN)
                 E SODIUM PHOSPHATE/DCN
                 E E4+ALL
L78
               O S L71 AND (E2 OR 1688/DRN)
               0 S L71 AND (E4 OR 1689/DRN)
L79
               O S L71 AND (E6 OR 1690/DRN)
L80
                 E SODIUM CHLORIDE/DCN
                 E E3+ALL
L81
               1 S L71 AND (E2 OR 1706/DRN)
                 E TRIS/DCN
                 E E3+ALL
L82
               0 S L71 AND (E2 OR 0418/DRN)
L83
               9 S L71 AND ((NA OR SODIUM)()(PHOSPHATE OR CHLORIDE) OR NACL OR T
               1 S L72 AND L81, L83
L84
L85
               9 S L72, L81, L83 NOT L84
               1 S L85 AND STABILISED HEPARINASE/TI
L86
               2 S L68, L86 AND L68-L86
L87
      FILE 'WPIX' ENTERED AT 17:43:07 ON 29 JAN 2002
      FILE 'DPCI' ENTERED AT 17:43:18 ON 29 JAN 2002
                 E US6187553/PN
L88
               1 S E3
                 E UW5262325/PN
                 E US5262325/PN
L89
               1 S E3
L90
               2 S L88, L89
```

FILE 'DPCI' ENTERED AT 17:44:26 ON 29 JAN 2002